

SUPPORTING INFORMATION

Supporting information contains one table and one figure.

Figure Legend:

Figure S1. Enzyme classes of **A**: the total drug target set (453) and **B**: those with phosphorylation within 12Å (132).

Table S1. All targets with endogenous cell MS evidence of phosphorylation near drug binding site. Entries in order of stage of development.

Target Protein	Uniprot Sequence ID	Stage of Drug Development	PDB ID	PDB Ligand ID	Phosphorylated Residue(s)	Distance (Å)
GTPase KRas (K-Ras)	P01113	Preclinical	4LUC	20G	Tyr64	6.8
p21-activated kinase 6 (PAK6)	Q9NQU5	Preclinical	4KS7	X4Z	Thr564	8.9
Serine/threonine-protein kinase PRP4 homolog (PRPF4B)	Q13523	Preclinical	4IJP	1EH	Ser837	9.6
Epidermal fatty acid-binding protein (FABP5)	Q01469	Preclinical	4AZM	T4B	Tyr131	2.7
Beta-Secretase 2 (BACE2)	Q9Y5Z0	Preclinical	3ZKQ	B3P	Tyr93	3.4
Tank-binding kinase 1 (TBK1)	Q9UHD2	Preclinical	4IM0	1FV	Tyr153	11.4
Cyclin-dependent kinase-like 3 (CDKL3)	Q8IVW4	Preclinical	3ZDU	38R	Tyr160	8.6
Ribosomal protein S6 kinase alpha-3 (Rsk2)	P51812	Preclinical	3UBD	SL0	Thr231	10.3
Mitogen-activated protein kinase 14 (MAPK14)	Q16539	Preclinical	3ZS5	SB2	Thr185	12.0
Serine hydroxymethyltransferase (Shmt1)	P34896	Preclinical	1EJI	THF	Tyr73	6.5
Glutathione reductase (GSR)	P00390	Preclinical	1XAN	HXP	Tyr451	3.5
Triosephosphate isomerase (TPI)	P60174	Preclinical	1HTI	PGA	S249	3.7
Phosphatidylinositol-3,4,5-triphosphate 5-phosphatase 2 (SHIP2)	O15357	Preclinical	4A9C	B5F	Tyr661	2.8
17beta-hydroxysteroid dehydrogenase type 10 (HSD10/ABAD)	Q99714	Preclinical	1U7T	TDT	Ser45	3.9
Protein tyrosine kinase 2 beta (PYK2)	Q14289	Preclinical	3FZS	B96	Tyr440	6.7
Spermine synthase (SMS)	P52788	Preclinical	3C6M	MTA	Tyr147	6.1
Creatine kinase B-type (CKB)	P12277	Preclinical	3B6R	CRN	Ser285	3.2
Ephrin type-A receptor 4 (EPHA4)	P54764	Preclinical	2Y6O	1N1	Thr692	2.9

Glycogen synthase kinase-3 beta (GSK3 β)	P49841	Preclinical	4AFJ	SJJ	Ser219	10.5
Tankyrase-1 (TNKS1)	095271	Preclinical	3UDD	34M	Tyr1292	7.4
Serine/threonine protein kinase Tao2 (TAO2)	Q9UL54	Preclinical	2GCD	STU	Tyr43	7.6
Hematopoietic cell kinase (HCK)	P08631	Preclinical	2HK5	1BM	Tyr330	7.0
Receptor-type tyrosine-protein phosphatase gamma (PTPG)	P23470	Preclinical	3QCG	NX1	Tyr1021	7.4
Calcium/calmodulin dependent protein kinase II alpha (CAMK2A)	Q9UQM7	Preclinical	3SOA	DB8	Ser25	6.3
Monoglyceride lipase (MAGL)	Q99685	Preclinical	3PE6	ZYH	Thr189	5.9
Heat shock cognate 71 kDa protein (HSPA8)	P11142	Preclinical	3LDQ	3P1	Tyr15	5.6
Activin receptor type-1 (ACVR1/ALK2)	Q04771	Preclinical	3OOM	507	Ser226	12.0
Calcium/calmodulin dependent protein kinase kinase II beta (CaMKK2)	Q96RR4	Preclinical	2ZV2	609	Tyr190	8.4
Aldo-keto reductase family 1 member C1 (AKR1C1)	Q04828	Preclinical	3C3U	C2U	Tyr24	3.8
Ephrin type-A receptor 3 (EphA3)	P29320	Preclinical	3DZQ	IFC	Tyr742	3.7
Ephrin type-A receptor 7 (EphA7)	Q15375	Preclinical	3DKO	IHZ	Tyr609	7.4
CDC-like kinase 1 (CLK1)	P49579	Preclinical	2VAG	V25	Ser341	12.0
Rac-beta serine/threonine protein kinase (Akt2)	P31751	Preclinical	2JDO	I5S	Thr313	8.1
Aldo-keto reductase family 1 member C3 (AKR1C3)	P42330	Preclinical	1ZQ5	E04	Tyr55	7.5
Rho-associated protein kinase 2 (ROCK2)	O75116	Phase I	2F2U	M77	Thr253	10.5
Arginase 1 (Arg1)	P05081	Phase I	2AEB	ABH	Ser230	9.3
Galectin-1 (LGALS1)	P09382	Phase I	3T2T	MQT	Ser30	4.4
Interleukin-1 associated receptor kinase 4 (IRAK4)	Q9NWZ3	Phase I	2NRU	T12	Thr209	7.4
Nicotinamide phosphoribosyltransferase (NAMPT)	P43490	Phase II	4LVF	20P	Tyr188	8.5
NT-3 growth factor receptor (TRKC)	Q16288	Phase II	3V5Q	0F4	Tyr705	9.5

Protein kinase C alpha (PKC α)	P17252	Phase II	3IW4	LW4	Thr501	10.1
Aurora A kinase (AURKA)	O14965	Phase II	3DJ6	AK6	Tyr148	6.8
Matrix metalloproteinase 2 (MMP2)	P08253	Phase II	1HOV	I52	Ser160	11.1
Protein kinase c beta II (PKCB)	P05771	Phase II	2I0E	PDS	Thr504	9.1
Aldo-keto reductase family 1 member B10 (AKR1B10)	O60218	Phase III	1ZUA	TOL	Ser23	10.0
Proto-oncogene tyrosine-protein kinase receptor Ret (RET)	P07949	Approved	2IVS	ACK	Tyr752	12.0
Vascular endothelial growth factor receptor 1 (VEGFR1)	P17948	Approved	3HNG	8ST	Tyr1053	11.9
Aldehyde dehydrogenase (ALDH3)	P30838	Approved	3SZB	I1E	Tyr186	9.0
Serine/threonine protein kinase MRCK beta (MRCK β)	Q9Y5S2	Approved	3TKU	M77	Ser363	11.6
Aldose reductase (ALDR1)	P15121	Approved	1US0	LDT	Tyr49	2.7
Adenosine deaminase (ADA1)	P00813	Approved	1NDY	FR3	Tyr67	12.0
Epidermal growth factor receptor (EGFR/HER1)	P00533	Approved	4G5J	0WN	Tyr764	9.6
Receptor tyrosine-protein kinase erbB4 (ERBB4/HER4)	Q15303	Approved	2R4B	GW7	Tyr733	6.7
Tubulin alpha 3C/D chain (TUBA3C)	Q13748	Approved	4EB6	VLB	Tyr210	3.1
Peptidyl-prolyl cis-trans isomerase FKBP5 (FKBP5)	Q13451	Approved	4DRI	RAP	Tyr54	10.3
Vascular endothelial growth factor receptor 2 (VEGFR2)	P35968	Approved	4AGD	B49	Tyr1053	10.7
Inosine-5-monophosphate dehydrogenase 2 (IMPDH2)	P12268	Approved	1JR1	MOA	Tyr411	2.8
Tubulin alpha-1A chain (TUBA1A)	Q71U36	Approved	1SA1	POD	Thr73	12.0
Anaplastic lymphoma kinase (ALK)	Q9UM73	Approved	3AOX	EMH	Tyr1131	6.3
Tyrosine protein kinase lyn (LYN)	P07948	Approved	2ZVA	1N1	Tyr265	11.8
Carbonic Anhydrase II (CA2)	P00918	Approved	3K34	SUA	Tyr51	12.0
Protein S100-A13 (S100A13)	Q99584	Approved	2KOT	ANW	Ser32	7.6

FIGURE S1

